DRAFT FOR DISCUSSION PURPOSES ONLY

REMARKS

Claims 1-20 are pending. Claims 1, 2, 4-8, 11 and 12 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Platz et al, U.S. Patent 5,418,130. Claims 1-17 are rejected under 25 U.S.C. § 103 (a) as being unpatentable over Platz et al, U.S. Patent 5,418,130. Claims 1-20 are rejected under obviousness-type double patenting as being unpatentable over claims 20-35 of U.S. Patent 6,093,725 in view of U.S. Patent 5,418,130.

Rejection under 35 U.S.C. § 102 (b)

Claims 1, 2, 4-8, 11 and 12 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Platz et al, U.S. Patent 5,418,130. Applicants' pending claims are to a method of treating red blood cells using a pathogen inactivating compound having a functional group that is electrophilic, wherein the electrophilic group can react covalently with the nucleic acid. The method further includes the use of a quencher comprising a nucleophilic group that can react covalently with the electrophilic group of the pathogen inactivating compound. Applicants have previously argued that these limitations are not suggested by Platz. While the Office Action correctly states that Platz teaches the covalent reaction of psoralens to nucleic acids, this well known photochemistry is the result of a cycloaddition of a double bond of the psoralen ring structure with a double bond of thymine or uracil in the nucleic acid, as shown in the schematic of columns 27-28 in Platz. This is a general reaction of the psoralen ring and does not involve the electrophilic group disclosed by Platz. Applicants maintain the argument that the electrophilic group of Platz does not react covalently with the nucleic acid. Platz indicates in column 4, line 27-31 that

> "The present invention utilizes a class of compounds based on 3-carboethoxy psoralens, psoralens, angelicins, khellins and coumarins which contain a halogen substituent and a water solubilization moiety, such as, quaternary ammonium ion or phosphonium ion."

The electrophilic group of Platz is added in order to improve water solubility of the compounds, not nucleic acid reactivity. In addition, these preferred compounds of Platz do not react according to the abovementioned psoralen cycloaddition as indicated in column 4, lines 35-39.

> "It is further advantageous in that only one photon of light is required to activate the brominated sensitizer, whereas two photons are required in sequential order of nonbrominated psoralens to complete classical phtoadduct DNA cross linking."

This mechanism of the reaction of the preferred psoralens in Platz is detailed in the schematic of columns 29 and 30, indicating that the reaction results in nucleic acid strand cleavage, not covalent addition of the psoralen.

With respect to Applicants' limitation of a quencher, the Office Action indicates that applicant has not demonstrated that the glutathione disclosed by Platz fails to act as recited in Applicants' claims. Applicants see no need to demonstrate this lack of activity when Platz clearly teaches the activity of the glutathione as an antioxidant. Column 26, lines 41-44 states

> "Antioxidants such as glutathione (an excellent hydrogen atom donor) may be added to the preparation to augment the red cell defenses *against free radical initiated damage.*" [emphasis added]

Further, the glutathione of Platz can not act as recited in the claims since Platz does not disclose an electrophilic group that can react with nucleic acid, as required by the claim. Finally, the invention of Platz teaches away from the use of an antioxidant quencher such as glutathione with the preferred electrophilic compounds disclosed (i.e. those compounds that have an electrophilic quaternary amine or similar group for improved water solubility). Column 6, line 28-48 states

> "In a preferred embodiment, the sensitizer will bear a charge, preferably a positively charged ammonium or phosphonium group, which can impart water solubility to the sensitizer molecule. The positive charge is preferably shielded, however, by substituents on the N or P atom which replace the acidic hydrogen atoms and which sterically shield the charge to disallow electrostatic binding to negatively charged species, such as cell membranes and proteins, to which binding of the sensitizer is undesirable. Thus, since the sensitizer will be bound primarily to target DNA/RNA, and not to cells or proteins, the likelihood of destruction of cells or proteins by the sensitizer upon irradiation is minimized.
>
> The psoralens (such as 8-MOP and AMT) must often be used in combination with a quencher (e.g. mannitol, vitamin E, etc.) to protect, repair or otherwise offset the deleterious effects of the sensitizer and light on cell membranes. The psoralen sensitizers herein do not accumulate in viral membranes and as a consequence do not require the presence of a quencher additive to the blood product."

This section further emphasizes a role of the electrophilic group of Platz that is not related to reactivity with nucleic acid (or quencher).

For the reasons stated above, Applicants feel that the Examiner's interpretation of Platz is misguided. Taken as a whole, Platz teaches psoralen derivatives that react differently than the classic psoralen pathway, i.e. that react by generating free radical damage to the nucleic acid rather than forming a cyclobutane addition to the psoralen ring. While Platz does discuss quenching, including the use of glutathione, the quenchers he refers to are antioxidants used to reduce oxygen radical damage from compounds that generate free radicals. There is nothing in Platz that suggests the limitations in Applicants' claims relating to an electrophilic group reacting with nucleic acid or a quencher. In fact, the preferred compounds of Platz teach away from using any quencher. Applicants respectfully request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 103 (a) over Platz

Claims 1-17 are rejected under 25 U.S.C. § 103 (a) as being unpatentable over Platz et al, U.S. Patent 5,418,130. The Office Action states that Platz discloses a pathogen-inactivating compound having the claimed structure that is quenched using glutathione. As discussed above, Applicants argue that Platz does not disclose a compound with an electrophilic group that can react with nucleic acid. The use of glutathione discussed in Platz was a general reference to its use as an antioxidant with certain psoralen compounds, and is unrelated to quenching per Applicants' claims. As discussed above, the invention of Platz teaches away from the use of such quenchers, therefore, disregarding that Platz does not teach compounds of Applicants' claims, there would be no motivation to develop quenchers at all. With respect to Applicants' prior arguments, the Office Action indicates that "While the reason for contacting the claimed sample with the claimed compounds and claimed quencher may be slightly different than that disclosed by applicant, as applicant is surely aware, claimed subject matter must be held obvious if the prior art suggests its practice, even if the prior art motivation is different than applicant's". As discussed above, Platz does not disclose all of the limitations to Applicants' claimed structure, i.e. the claimed compounds are not disclosed by Platz. The reason for contacting compounds disclosed in Platz with a quencher is different from Applicants' reasons because Applicants' compounds are different. Applicants respectfully request that this rejection be withdrawn.

Rejection under obviousness-type double patenting

Claims 1-20 are rejected under obviousness-type double patenting as being unpatentable over claims 20-35 of U.S. Patent 6,093,725 in view of U.S. Patent 5,418,130. For the reasons discussed above, in particular that Platz teaches away from using a quencher, Applicants feel that Platz would not motivate the artisan of ordinary skill to consider the general idea of an antioxidant quencher disclosed in Platz to be effective in Applicants' unrelated system.

Applicants believe that the present claims and those of 6,093,725 are patentably distinct and respectfully request that the obviousness-type double patenting rejection be withdrawn.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicant's claims are in condition for allowance and such allowance is earnestly solicited.

The Assistant Commissioner is hereby authorized to charge any additional fees associated with this petition or credit any overpayment to **Deposit Account No. 19-4315. A duplicate copy of this petition is enclosed for that purpose.**

Respectfully submitted
CERUS CORPORATION

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By: _____

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